pill and other preparations of arsenic; the hypodermic injection of liquor potassæ; quinine, ipecacuanha, *Aristolochia indica*, and a variety of other drugs, generally of a vegetable nature, and enjoying a large amount of popular confidence: all, when brought to the test of carefully conducted experiment, failed, as might have been expected, to give any favourable result.

It seems almost unnecessary to allude to the so called snake-stones; they are powerless for good or evil. They have also enjoyed much confidence; but when submitted to the test of impartial experiment and observation, their virtues prove as unreal as those of the antidotes above mentioned.

With reference to the mechanical methods of preventing the entry of the poison into the circulation after a bite, we think that the speedy application of an elastic cord (such as is used in bloodless operations) round the limb, combined with the application of cups attached to an exhausting-syringe or pump*, might be of advantage, and that it might be made of general application in India.

January 29, 1874.

JOSEPH DALTON HOOKER, C.B., President, in the Chair.

The Presents received were laid on the Table, and thanks ordered for them.

The following Papers were read:—

I. "Contributions to the Normal and Pathological Anatomy of the Lymphatic System of the Lungs." By E. Klein, M.D., Assistant Professor at the Laboratory of the Brown Institution, London. Communicated by Professor J. B. Sanderson, F.R.S. Received November 13, 1873.

I propose to give in the following pages a summary of an investigation of the lymphatic system of the lungs, in the normal condition as well as in chronic secondary inflammation, undertaken in connexion with the pathological inquiries of Dr. Burdon Sanderson, for the Medical Department of the Privy Council. The research will be published at length during the course of the next year, in continuation of my work 'On the Anatomy of the Lymphatic System,' of which the first part, "Serous Membranes," has recently appeared. The present communication is made with the approval of the medical officer of the Privy Council, Mr. Simon.

A. *Normal conditions.*

(*a*) The endothelium of the surface of the lungs consists, in the normal

(animal, vegetable, and mineral) that have been administered as antidotes. Particulars may be found in the 'Thanatophidia,' where the details of experiments conducted for the investigation of their actions are recorded.

* Such an apparatus has now been constructed.

condition, of polyhedral cells (not flattened as commonly described) arranged in a single layer. This is well seen in guineapigs, less distinctly in rabbits, rats, dogs, and cats. If the lung is not distended, the endothelium of the surface very much resembles an epithelium, the cells being polyhedral, or in the form of short columns; they are markedly granular, and have distinct nuclei. Even in the moderately distended lung, the endothelium of the pleura pulmonum is by no means of the same morphological character as that on the costal pleura. Between the endothelium of the one and that of the other organ there exists the same difference as between that of the ovary and that of the peritoneum—the one consisting of polyhedral, or shortly columnar, granular cells with very marked nuclei, the other of very flattened, almost hyaline, endothelial plates.

(*b*) The pleura pulmonum is a very thin connective-tissue membrane, provided, like other serous membranes, with a rich network of elastic fibres. In the lungs of the rat, rabbit, cat, and dog the pleura pulmonum seems to consist, for the most part, of elastic networks. In the matrix, there is generally one layer of flattened connective-tissue corpuscles to be found.

Beneath the proper pleural membrane, there exists, in the guineapig, a membrane which consists of non-striated muscular fibres, arranged in bundles which form a meshwork. In the normal condition the bundles are relatively thin, and the meshwork which they form has elongated large meshes. In the distended lung the meshes are of a much greater diameter than in the collapsed lung; in the latter they form a more continuous membrane. The muscular bundles have, in general, a radiating direction from the apex towards the basis of the lung; and it is further to be noted that they are most abundant on the external surface, viz. that directed towards the anterior wall of the chest, and the internal surface, viz. that directed towards the mediastinum; whereas on the posterior surface the bundles are scanty, and become more and more so the nearer the vertebral column is approached. This distribution of the muscular tissue is therefore in perfect agreement with the proportion in which the different parts of the lung participate in the respiratory movement, the fibres being most richly distributed over those parts of the pulmonary surface which are subject to the greatest extent of excursions, and *vice versâ*. In rats and rabbits, as well as in cats and dogs, bundles of unstriped muscular fibres occur sparingly; at any rate there are none on the posterior surface of the lung of these animals. As soon as the superficial parts of the lung become the seat of a chronic inflammatory process (*e. g.* tuberculosis, chronic pneumonia), the muscular bundles increase in breadth and number to such a degree, that they form a continuous membrane, chiefly in those parts of the surface which correspond to the diseased portions of the lung.

1. *Subpleural lymphatics.*—The meshes of the muscular membrane of the lung of guineapigs are lined by a single layer of flattened endothelial cells, constituting, in fact, a communicating system of lymphatic sinuses.

I call this system of lymphatics the *intermuscular or pleural lymphatics*. In the distended lung of the guineapig, these pleural lymphatic sinuses are seen to be covered by hardly any thing but the endothelium of the pleural cavity, between which and the cavities of those sinuses a free communication exists by means of true stomata; so that the endothelium lining the sinuses is here directly continuous with that of the pleural surface. In every case of chronic pleuritis induced by injecting irritating substances (such as products of acute and chronic pyæmic processes, products of indurated lymphatic glands), an active germination of the endothelium around those stomata takes place. This germination extends not only to the endothelium of the neighbouring parts of the pleural surface, but also to the endothelium of the intermuscular lymphatic sinuses. The relation between the cells of the membrana propria of the pleura pulmonum and the endothelium of the surface is similar to that already described by me in other serous membranes, the cells of the *propria* throwing out processes, which project between the endothelial elements of the free surface, thus forming pseudostomata. The pleural lymphatics stand in communication with lymphatic tubes, which lie in grooves, the arrangement of which corresponds with that of the most superficial groups of alveoli of the lung. These may be called the *subpleural lymphatics*; they are provided with valves, and form a network of anastomosing lymphatic vessels. The larger trunks run along the ligamenta pulmonum towards the root of the lung. This system of lymphatic vessels is best developed in the lung of the dog, in which it has been described by Wywodzoff; it is also well developed in the lungs of rabbits and cats. It receives lymphatic branches, which take their origin between the alveoli of the superficial portions of the lung. The mode of origin of these interalveolar lymphatics is that already described in my published work. The septa of the alveoli contain branched connective-tissue corpuscles; the spaces in which these cells lie, forming the lymphcanalicular system, open into the cavities of the interalveolar lymphatics, with the endothelium of which the cells of the lymphcanalicular system are in direct continuity.

2. *Perivascular lymphatics.*—Besides the system of subpleural lymphatics, the lung contains two other systems; of which one takes its origin in the alveolar septa from branched cells exactly like those previously referred to. The lymphatic capillaries of this system lead into vessels that accompany the branches of the pulmonary artery and vein; they run either in the adventitia of these vessels in twos or threes, anastomosing with each other, or the blood-vessel is entirely, or only half, invaginated in a lymphatic vessel. The branched cells of the alveolar septa, from which the capillaries of this system of lymphatics (which we will call the *perivascular lymphatics*) originate, have an important relation to the epithelium of the alveoli; for they send a process, or a greater or less portion of their body, between the epithelial cells into the cavities of the alveoli. These represent pseudostomata, as described by myself for the serous

membranes. As these branched cells have a corresponding lymphcanalicular system, it is easy to understand why Sikorski, in his experiments, found that carmine entered freely from the cavities of the alveoli into the interalveolar lymphatics. But there is no other communication between the cavities of the alveoli and the lymphatics than by means of these pseudostomata. It can be easily understood that the pseudostomatous canals (viz. the canal in which lies the process of a cell projecting freely into the cavity of an alveolus, and the lymphcanalicular system, in which the interalveolar branched cells lie) may become occasionally distended, *e. g.* in inflammation, by exudation, or by migratory cells. In fact, it must be assumed that cells, such as are produced by catarrhal inflammation of the air-passages, migrate from the cavities of the alveoli into the interalveolar lymphcanalicular system through those pseudostomata; and the same assumption must be made for the well-known large granular mucous corpuscles, in many lungs, containing carbon particles, inasmuch as similar cells are found in the interalveolar tissue.

3. *Peribronchial lymphatics.*—The third system of lymphatics is composed of lymphatic vessels which are chiefly distributed in the adventitia of the bronchi. I shall therefore call it the system of *peribronchial lymphatics*. The vessels of this system are usually distributed around the bronchi, anastomosing with each other, and especially with the perivascular lymphatics. The vessels of the peribronchial system take up capillaries, which originate in the mucous membrane of the bronchi and penetrate through the tunica muscularis of the bronchi. These capillary branches originate in the usual way; *i. e.* their wall is continuous with the branched cells of the mucosa, which cells in turn penetrate, as a nucleated reticulum, between the epithelial cells of the bronchus, and project on its free surface. From this it may be understood how particles can penetrate from the cavity of a bronchus into the peribronchial lymphatics, as in the experiments of Sikorski. The lymphatics are always most numerous on that side of a bronchus which is directed towards a branch of the pulmonary artery. In the course of each bronchus, especially those that possess only a thin muscular tunic and no trace of cartilage, there are generally several vasculated lymph-follicles to be met with, which are placed in continuity with the endothelial wall of a lymphatic vessel, in such a manner that they are surrounded by that lymphatic vessel, in the same way as the lymph-follicles of Peyer's patches are by their lymph-sinuses. These follicles, already seen by Dr. Burdon Sanderson, extend up to the tunica muscularis; in some instances they are to be traced through this latter into the mucosa. They always lie in the wall of a lymphatic vessel, between the bronchus and the accompanying branch of the pulmonary artery. They are of different sizes, and are generally spherical or elliptical; sometimes they represent merely a cord-like thickening of the wall of the lymphatic vessel. In the lung of the guineapig these perilymphangial follicles are very numerous; they are not so numerous in rabbits. It can be proved that

a constant growth and reproduction of these follicles is going on. The lymphatic vessels of the two last-mentioned systems anastomose with each other in the ligaments of the lung, and finally enter the bronchial lymphatic glands.

B. *Pathological conditions.*

I have already mentioned the germination of the endothelium of the surface, and the hypertrophy of the muscles, in chronic diseases of the lung.

In many chronic inflammatory processes of the lung (chronic pyæmia, artificial tuberculosis, chronic pneumonia) the pleura pulmonum becomes the seat of nodules of various sizes and shapes. Generally they are more or less round, and correspond in position to those superficial portions of the lung which have become the seat of an inflammatory process. These nodules of the pleura are due to a very rapid proliferation of the branched connective-tissue corpuscles, simultaneously with an increase of fibrous connective tissue, this latter fact being very obvious when the nodules have reached a certain age. As long as they are small, they show merely an abundance of cellular elements; in their later stages they become richly supplied with capillary blood-vessels.

Lungs of guineapigs that are far advanced in the process of artificial tuberculosis (*i. e.* where the bronchial glands have already become the seat of cheesy deposits) show superficial nodules, which are in direct continuity with the subpleural lymphatics. In horizontal sections through such portions of the lung, one finds these lymphatics filled with lymph-corpuscles, while at a later period they are occupied by an adenoid reticulum, the meshes of which contain lymph-corpuscles, and which is in direct continuity with the endothelium of the lymphatic tubes. The nodules themselves represent a network of cords, which very much resembles adenoid tissue. The meshes of this network of trabeculæ are the alveoli, which, at an early period, contain a few lymphoid corpuscles, while the epithelium is, at the same time, in a state of germination, the individual cells being swollen and the nucleus in a state of division. At a later period the alveoli are filled with small lymphoid corpuscles, while the epithelium of the alveoli is no longer to be distinguished as such. The blood-capillaries belonging to these alveoli have undergone some remarkable changes, of which I shall speak at length afterwards; at present I will only mention that at a later period they are no longer permeable for the blood. These interalveolar trabeculæ of adenoid tissue, forming the framework of the superficial nodules, are developed from the branched connective-tissue corpuscles of the alveolar septa. The same process extends to the subpleural lymphatics, originating from these interalveolar connective-tissue corpuscles, in such a way that these lymphatics become converted into cords of adenoid tissue connected with their endothelium. Consequently these lymphatics become converted into endolymphangial cords.

If one examines the lungs of a guineapig which is so far advanced in the process of artificial tuberculosis that the bronchial glands contain cheesy deposits, one can distinguish with the naked eye two kinds of morbid structure on the surface of the lungs:—

(*a*) Translucent structures of a circular or irregular shape, sometimes projecting slightly above the surface, generally isolated, but in some instances confluent, so as to form patches. The smallest are of the size of the head of a small pin; some of them are three, four, or several times as large. In some lungs only the large structures are to be found; the larger kind have generally a yellowish centre.

(*b*) Opaque patches of considerable diameter projecting above the surface of the lung, some of them relatively very large (about $\frac{1}{6}$ to $\frac{1}{10}$ of an inch), quite white, and very firm. On sections through the lung one finds that the first kind of structures correspond with cords provided with lateral nodular swellings, which accompany the branches of the pulmonary artery and vein. The second kind of structures correspond with nodules and patches which are irregularly distributed in the tissue of the lung. On microscopical examination it is seen that the first kind of structures are perivascular cords of adenoid tissue, representing the follicular tissue which is found in the walls of the peribronchial lymphatics in the normal condition. Many of these perivascular cords or nodules are supplied with a system of capillary blood-vessels. The second kind of nodules, or patches, are seen to consist, on microscopical examination, of a framework of trabeculæ which corresponds to the interalveolar tissue; they represent trabeculæ of adenoid tissue which are in continuity with the perivascular cords first mentioned. The meshes of this network are more or less filled out by cells lying in the spaces that were previously the cavities of the alveoli. The question arises, How do these two kinds of morbid structures develop, and what is their ultimate fate?

If one studies sections of lungs that possess very few of the first kind of cords and nodules, one comes across a number of the lymphatic vessels that accompany the branches of the pulmonary artery, containing more or less numerous lymph-corpuscles. In addition to those just mentioned, one is able to find lymphatic vessels, the endothelium of which is in continuity with a thin short cord of adenoid tissue that stretches along the outer wall of the lymphatic, or (as may be seen in some places) projects into its cavity, thus connecting the two endothelial walls of the lymphatic; in other words, we have here a peri- as well as an endolymphangial growth of adenoid tissue, connected with the endothelium of the lymphatic. From what I have shown in the case of the serous membranes, there can be little doubt that the above-mentioned tuberculous cords of adenoid tissue accompanying the blood-vessels are in reality only peri- or endolymphangial outgrowths of the endothelium of the lymphatics. It is important to state that, at the same time, the follicles of the bronchial adventitia increase in size, and also that a perilym-

phangial new growth takes place on the peribronchial lymphatics. From the study of the normal lung, it can be ascertained that not all the large branches of blood-vessels are accompanied by lymphatics, and not even one and the same branch for its whole length, but that in some places they are only surrounded by branched connective-tissue corpuscles, which may be said to belong to their adventitia. In a given case, one will not be able to determine whether a certain tubercular cord has developed by the increase of these adventitial cells, or whether it has developed from the endothelium of a lymphatic, either as a peri- or endolymphangial cord; for the fully developed cords have quite the same relation to the blood-vessels as if they had developed in their adventitia.

I have already mentioned that the growth of adenoid tissue in the branches of the subpleural lymphatics extends to the connective-tissue corpuscles between the alveoli. Exactly in the same way we see the perivascular adenoid cords spreading between the alveoli; that is to say, the perilymphangial growth of tracts of adenoid tissue extends from the lymphatics to the interalveolar branched cells, with which the endothelium of the former is in direct continuity.

The first points at which the tubercular perivascular cords of adenoid tissue make their appearance are the ultimate branches of the pulmonary artery and vein, whence they spread along the lymphatics towards the larger branches, as well as towards the interalveolar branched cells. In general the growth in the first direction (that is, towards the larger branches) goes on much more abundantly and rapidly than in the other direction.

It is an important fact that I have constantly met with the following condition of the tuberculous lungs of guineapigs:—The ultimate branches of the pulmonary artery show a germination of their endothelium, which is already recognizable in the earlier stages of the disease, at a time when perivascular cords are only rarely to be found. If the process advances, the germination of that endothelium reaches such a degree that the cavities of the blood-vessels are almost filled with its products, only a very narrow central canal being left free. In later stages, the tunica media of the smaller and middle-sized vessels, that are provided with perivascular cords, becomes very much thickened, and splits into laminæ, between which lie accumulated lymphoid cells, either free or contained in a reticulum. In many places it can be shown that the adenoid tissue of the perivascular cords gradually grows towards the cavities of the vessels, and finally assumes the whole portion of the vessel into its substance. The chief fact of importance, however, is that the capillary blood-vessels of those interalveolar trabeculæ, into which the perivascular cords have penetrated, have become converted into solid nucleated bands and threads, which are in continuity with the surrounding reticulum. These threads, although they appear solid, must be taken as still permeable by fluid substances; for in lungs the pulmonary artery of which had been previously injected with a cold

solution of Berlin blue, the cavity of many of the capillaries in the neighbourhood of those interalveolar trabeculæ stops short, but the injecting material can be traced into the nucleated filaments which enter those trabeculæ. From the study of a great number of specimens, taken from lungs in different stages of the process of artificial tuberculosis, I have reason to believe that the first parts which undergo inflammatory changes are the ultimate branches of the pulmonary artery and the capillaries next to them, and that the morbid process extends from them to the corresponding lymphatics.

I have already mentioned that, where the alveolar septa become thickened, the epithelium of the alveoli becomes gradually changed, so as completely to fill the cavities of the alveoli. By this means nodular or patch-like structures are formed, which may be called secondary patches. It may be said, in general, that the epithelial cells proliferate: they enlarge; their nuclei divide; and then the cells themselves divide. In many alveoli there appear, besides isolated epithelial cells, with or without carbon particles in their substance, numerous small lymphoid corpuscles. In some of the alveoli the enlarged epithelial cells become fused together to one large mass of granular protoplasm, which contains a number of nuclei in its periphery; this represents, in the true sense of the term, a "giant cell." We may therefore say that, at an early period, these patches consist of trabeculæ, which represent the thickened interalveolar septa and their meshes (the alveoli), and that the latter are filled either with small cells or with giant cells, or rather with multinuclear protoplasmic cylindrical masses. These secondary patches gradually increase in size, by the extension of the adenoid metamorphosis of the alveolar septa and the changes of the capillary blood-vessels, indicated above.

A perivascular cord may become furnished with a number of lateral nodules of adenoid tissue from the assumption, by adenoid interalveolar cords, of the contents of alveolar cavities into their own tissue. Where, however, the alveolar cavities contain giant cells, other remarkable changes take place. These are as follows:—The cylinders of multinuclear protoplasm grow and divide into a number of giant cells, which gradually become converted into a tissue to a certain extent resembling adenoid tissue, but differing from it in many respects. Thus the giant cells give origin to a more or less regular network of nucleated cells, which, consisting at first of granular substance, soon assume the appearance of a more or less distinct fibrillar substance; in their meshes lie only a limited number of lymphoid cells. This tissue spreads very rapidly, and finally undergoes, from the centre outwards, a fibrous degeneration, which becomes the seat of cheesy deposits.

Different lungs are somewhat different in this latter respect. In some cases the transformation of the giant cells into a network of nucleated cells goes on very rapidly; and then the cheesy metamorphosis is also soon established. In other cases the growth of the network of nucleated cells

has a very long duration, and consequently the growth of the secondary patches remains active for a long time. The network of nucleated cells is, at no period of its development, such a delicate reticulum as in the adenoid tissue, nor does it contain lymphoid corpuscles so regularly as this latter. Moreover the adenoid tissue of the perivascular cords or their lateral nodules *never becomes the seat of a fibrous or cheesy metamorphosis.* The more the lung has advanced in the process of artificial tuberculosis, the more do we find the tissue of the lung, in the neighbourhood of the primary and secondary nodules, undergoing inflammatory changes—consisting in thickening of the alveolar septa, and in a granular condition of the walls of their capillary blood-vessels, the nuclei of which are in active proliferation, their number being out of proportion large.

In the peripheral parts of the lung the most numerous secondary nodules are to be met with; and consequently the most numerous cheesy deposits are here to be found. I have often seen a system of large patches projecting somewhat above the surface and radiating towards the deeper parts, as the terminal branches of a minute bronchus pass towards the stem.

The secondary process extends from the terminal branches (alveoli and infundibula) to the large bronchi. In these the process becomes very marked, and consists of the following changes:—

(*a*) The epithelium proliferates very abundantly, whereby the cavity may finally become almost completely plugged up by the progeny of the epithelium.

(*b*) A more important change consists in the proliferation of the tissue that we have designated above as pseudostomata, namely the branched cells of the tunica mucosa that extend between the epithelial cells to the surface; this tissue grows so as to form a very rich adenoid tissue. At the same time there goes on an active growth of adenoid tissue in the walls of the peribronchial lymphatics; that is to say, there is a hyperplasia (Sanderson) of the preexisting follicles, as well as a new formation. [The most active transformation of the pseudostomatous tissue of the bronchi into adenoid tissue I have met with was in rabbits suffering from chronic pyæmia; it has been already stated that the reticulum of branched cells which stretches between the epithelial cells of the surface is better developed in rabbits than in guineapigs, in the normal condition.]

(*c*) In the large bronchi, which have become involved in the secondary process, another noteworthy change takes place, viz. the fusion of groups of the proliferating epithelial cells, not only those of the free surface, but also those of the mucous glands, so as to form multinuclear protoplasmic cylinders and lumps (giant cells).

The secondary process, viz. that which affects the alveoli and bronchi, and which may be justly called the catarrhal pneumonic process, always accompanies artificial tuberculosis when it has extended to the

interalveolar tissue; in the early stages of artificial tuberculosis, *only the perivascular lymphangial cords are to be met with.*

If the infection has been established from the pleural cavity, the germination of the endothelium of the surface round the stomata, and the transformation of the subpleural lymphatics into cords of adenoid tissue, is the first symptom, and is followed by the appearance of perivascular adenoid cords. If, however, the lung becomes tuberculous by infection from the blood-vessels, the peritoneal cavity or the subcutaneous tissue, the perivascular adenoid cords are the first structures that make their appearance. In lungs which have become the seat of chronic pyæmia, the first changes are to be found in the alveolar septa and alveoli, viz. the formation of patches and nodules similar to those that I have designated before as secondary; and if the process lasts long enough, those changes take place that I have designated before as primary tuberculous changes.

The opinion has been expressed (by Sanderson and Wilson Fox) that the process of artificial tuberculosis in the lungs of guineapigs resembles, in its anatomical features, the tuberculous process in man. I will therefore examine the process that is clinically and anatomically known as miliary tuberculosis in man. For this purpose I shall describe the changes that I found in three series of cases of miliary tuberculosis in children, representing, as we shall see, three different stages of development. In the first series the lungs exhibited all the anatomical appearances of acute miliary tuberculosis. On microscopical examination it was found that the nodules were due to groups of alveoli (with the corresponding infundibula) being filled with and distended by a fibrinous material that contained granules and a few small cells; generally these latter occupied the centre of the alveoli. The walls of the alveoli were hardly distinguishable; and the capillary vessels were not permeable, as shown by the fact that, in well-injected preparations, the injection did not penetrate into the capillaries of the alveolar septa. The alveoli next to these nodules contained the same fibrinous material; but they were not filled up by it completely; and their epithelium could be distinctly recognized, having become wholly or partially detached, the individual cells being somewhat enlarged, and some of them containing two nuclei. Here the injection material penetrated the capillary blood-vessels more or less perfectly: the alveoli of the neighbouring parts contained either a small amount of fibrinous material, besides isolated young cells, or a homogeneous gelatinous substance that had become stained with hæmatoxylin. The epithelium was very distinct, its cells granular. In some of the alveoli the epithelial membrane was more or less detached from the alveolar septa; the capillary blood-vessels were perfectly permeable.

In the second series of cases of miliary tuberculosis, in which the lungs did not differ in macroscopical appearance from those of the first series, but in which the process had lasted longer, the microscopical appearances were

somewhat different. The nodules were seen to differ in their structure from those in the former series in the following respects. In some of them it was easy to recognize that they represented a number of alveoli very much distended by a fibrinous substance similar to that described above, which included granular material and a number of small cellular elements; the trabeculæ of these nodules (that is, the interalveolar tissue) were slightly thickened and contained young cells, their capillary blood-vessels being not completely permeable and not easily distinguishable. Besides these there were nodules of which only the central alveoli were in the state just mentioned; whereas in those situated more peripherally the fibrinous material was no longer to be discovered, but they were filled in one or other of the following ways:—first, by spherical nucleated elements, many of which could be still recognized as epithelial cells, by their size, granulation, and nucleus, and some of which contained two nuclei. In these places, the interalveolar trabeculæ were thickened in a very marked manner, exhibiting all the appearances of an infiltrated tissue—that is to say, a more or less distinct reticulum of nucleated fibres, in the meshes of which lay small lymphoid corpuscles very readily stained by logwood or carmine. Or, secondly, they were filled by one large multinucleated mass or giant cell. In the latter case the giant cell, or rather the multinuclear protoplasmic cylinder, contained the nuclei either regularly distributed in its periphery, or all crowded together in the central part of the mass. As regards the nuclei, it may be said that they stain readily; they are relatively small, sharply outlined, and contain one or two nucleoli. The protoplasm of the giant cell is tinted slightly yellowish, does not stain in hæmatoxylin, and is very regularly filled with small granules of equal size. As regards the development of these giant cells and their nuclei, I must first contradict those authors who say that they originate generally by a free-cell formation in the veins, as well as those who make them originate in lymphatic vessels; for I have followed their development from the epithelial cells of the alveoli with all possible certainty. I have been able to make out that the whole epithelial lining of an alveolus becomes fused together into one protoplasmic lump which fills out the alveolar cavity, and the nuclei of which rapidly divide, remaining, however, in their original places, viz. peripheral. We have here a protoplasmic cylinder the transverse section of which shows a peripheral ring of nuclei. But a single epithelial cell may also become transformed into a multinuclear giant cell: one or the other epithelial cell increases rapidly in size (probably at the expense of its fellows); its protoplasm becomes enlarged as well as its nucleus; then this nucleus gives rise by cleavage, or by budding, to a number of small nuclei, so that it is transformed into a number of nuclei lying in the middle of the cell. [I have little doubt that Klebs would be much inclined to regard the very regular granulation of the giant cells previously mentioned, as being due to the presence of micrococci; such an assumption, however, could not easily be proved. A substance filled very regularly

with granules is said to be filled with micrococci. Against that view, however, it can be maintained, first, that there are a number of normal tissues that appear after hardening to be just as regularly filled with granules (*e. g.* the liver-cells of any liver hardened in spirit), and, secondly, that the resistance of these granules to acids and alkalies after hardening does not prove them to be micrococci.]

Where the alveoli contain giant cells, the alveolar septa are very much thickened, and are seen to consist of a tissue that contains branched and spindle-shaped cells, the substance of which has more or less the appearance of a fibrous tissue, their processes as well as their body being slightly fibrillar. Between these there are very few lymphoid corpuscles to be found.

In a third series of lungs, which also in macroscopical aspect did not differ from the former ones, it is seen that almost all the nodules contain giant cells, corresponding to the alveolar spaces. These, however, have undergone changes which are correctly described by Schüppel and others; viz. the giant cells give origin to a network of branched nucleated cells, as well as to a few spherical nucleated elements that lie in its meshes. This network grows at the expense of the giant cell, which undergoes proliferation at the same time. We have here what is generally called a reticular tubercle. From one giant cell a number of giant cells may take their origin.

The nearer to the centre of a nodule the giant cell lies, the more extensively and quickly does a transformation of its substance take place. It becomes converted into a very dense feltwork of fibrillar tissue, the nuclei of which gradually disappear, while the tissue itself dies away, becoming firm and hard, and finally resembling a granular substance, in which fibrils can be made out very indistinctly. While the network of the nucleated cells continues to grow at the expense of the giant cells, the process of necrosis spreads gradually to the peripheral parts. In this stage of the process the thickened interalveolar trabeculæ become also assumed into, and identified with, the tissue that originated from the giant cells. In the neighbourhood of the nodules there are very numerous places where the interalveolar trabeculæ are thickened and contain numerous young cells, the epithelium of the corresponding alveoli being, at the same time, in a state of proliferation. In general the tubercular nodules of both these latter series have the common character that the peripheral zone of the tubercular nodule is a regular adenoid tissue, being composed of a delicate reticulum which includes small lymphoid corpuscules; this adenoid tissue is in continuity with the tissue of the interalveolar trabeculæ above mentioned. In these stages of the tuberculous process, we find numerous branches of large blood-vessels, in the immediate neighbourhood of the nodules, provided with the same perivascular cords of adenoid tissue as have been described in the tuberculous lung of the guineapig.

Finally, it may be mentioned that these nodules also grow in circumference, by the alveolar septa of the neighbouring alveoli gradually becoming thickened, while, at the same time, the epithelium of the corresponding alveoli undergoes the changes before described. The capillary vessels of these parts show the same changes as were mentioned in the case of the guineapig's lung—being transformed gradually into nucleated fibres, which must be supposed to be, for a certain time, still permeable by coloured fluids.

If we summarize the results thus described, it is evident that the changes in the process of miliary tuberculosis in man are only to a limited extent similar to those which occurr in the process of artificial tuberculosis in guineapigs. In the lung of tuberculized guineapigs the first structural changes are characterized, briefly speaking, by the appearance of perivascular lymphangial nodules, whereas the changes of the interalveolar tissue and the alveolar epithelium form only a secondary process. In miliary tuberculosis of man, on the other hand, we see that the first changes take place in the alveoli and interalveolar septa, and these changes are followed by the appearance of perivascular cords.

It is therefore probable that, in artificial tuberculosis of the lung of the guineapig, the parts first attacked are the small branches of the pulmonary artery or pulmonary vein, whereas in the miliary tuberculosis of man the capillary blood-vessels of the alveoli seem to be the tissue from which the action of the morbid agent starts.

II. "On the Comparative Value of certain Geological Ages (or groups of formations) considered as items of Geological Time." By A. C. Ramsay, LL.D., V.P.R.S. Received December 16, 1873.

(Abstract.)

The author first reviews briefly several methods by which attempts have been made to estimate the value of minor portions of geological time, such as:—calculations intended to estimate the age of deltas, founded on the annual rate of accumulation of sediments; the astronomical method followed by Mr. Croll, in connexion with the recurrence of glacial epochs; the relative thicknesses of different formations; and the relation of strong unconformity between two sets of formations in connexion with marked disappearance of old genera and species, and the appearance of newer forms. Having shown that none of these methods give any clear help in the absolute measurement of time in years or cycles of years, even when founded on well-established facts, he proceeds to attempt to estimate the *comparative value* of long portions of geological time, all of which are represented by important series of formations.